

**CLAIMS:**

1. A method of analysing the genetic characteristics of a reproductive tract cell sample taken from a subject, the method comprising the steps of:
  - (a) taking a cell sample from the subject
  - 5 (b) isolating one or more target cells from the sample; and
  - (c) analysing the genetic characteristics of the one or more target cells isolated from the sample.
2. A method as claimed in claim 1, in which the subject is a mammal .
3. A method as claimed in either of claims 1 or 2 in which the subject is a human being.
- 10 4. A method as claimed in either of claims 1 or 2, in which the subject is a non-human animal.
5. A method as claimed in any of the preceding claims, in which the one or more target cells are of embryonic origin.
- 15 6. A method as claimed in claim 5, in which the one or more target cells are fetal cells.
7. A method as claimed in any of the preceding claims, in which step (a) comprises a non-invasive or substantially non-invasive procedure.
8. A method as claimed in claim 7 in which the cell sample is taken by using an endocervical brush or a cytobrush to gather a cell sample from the subject by scraping the lining of the cervix or reproductive tract.
- 20 9. A method as claimed in claim 8, in which the reproductive tract cell sample is:
  - (a) a cervical cell sample; or
  - 25 (b) a high vaginal smear.
10. A method as claimed in claim 9, in which the reproductive tract cell sample is taken via a Pap smear procedure.

11. A method as claimed in claim 10, in which the Pap smear procedure is either:
- (a) a thin section Pap smear procedure; or
  - (b) a thick section Pap smear procedure.
- 5 12. A method as claimed in either of claims 10 or 11 when appended to claim 3, in which the reproductive tract cell sample is obtained via a Pap smear procedure performed at between 5 and 31 weeks gestation.
13. A method as claimed in claim 12 in which the method is performed in the first or second trimester of gestation.
- 10 14. A method as claimed in any of the preceding claims, in which the cervical cell sample additionally comprises one or more of the following:
- (a) blood; and
  - (b) vaginal cells.
- 15 15. A method as claimed in any of the preceding claims, in which step (b) of claim 1 comprises an enrichment procedure, to isolate one or more target cells from other cells present in the reproductive tract cell sample.
16. A method as claimed in claim 15, in which the enrichment procedure comprises either or both:
- 20 (a) a positive enrichment procedure, whereby one or more target cells are extracted from the cell sample by differentiation according to antigen expression (or non-expression) in those cells; and
  - (b) a negative enrichment procedure, whereby one or more non-target cells are differentiated from target cells by using identification means and the non-target cells are then removed from the reproductive tract cell sample.
- 25 17. A method as claimed in claim 15, in which the enrichment procedure comprises the use of one or more of the following techniques to differentiate target cells from non-target cells in the reproductive tract cell sample:

- (a) exploitation of differences in physical cell characteristics;
  - (b) exploitation of biological differences between cell types; and
  - (c) exploitation of genetic differences between cell types.
- 5 18. A method as claimed in claim 17, in which the technique used to differentiate between target and non-target cells in the reproductive tract cell sample is technique (a), and the differentiation step comprises the use of one or more of the following:
- (a) exploiting physical differences between cells in the reproductive tract cell sample;
  - 10 (b) exploiting differences in morphological characteristics as between cells in the reproductive tract cell sample;
  - (c) exploiting differences in the granularity characteristics as between cells in the cervical cell sample;
  - 15 (d) exploiting differences in DNA content as between cells in the reproductive tract cell sample ;
  - (e) density separation;
  - (f) fluorescence activated cell sorting;
  - (g) magnetic activated cell sorting ;
  - (h) cell lysis;
  - 20 (i) complement-mediated lysis;
  - (j) flow cytometry;
  - (k) panning;
  - (l) charge-flow separation and/or
  - (m) laser microdissection.
- 25 19. A method as claimed in claim 17, in which the technique used to differentiate between the target and non-target cells in the cell sample is

technique (b) and the differentiation step comprises the use of one or more of the following:

- 5 (a) exploiting immunological differences between target and non-target cells in the reproductive tract cell sample; and/or
- (b) cell culture methods that promote selective propagation of the cells sought to be isolated.
20. A method as claimed in claim 17, in which step (a) is used and the target and non-target cells in the reproductive tract cell sample are differentiated by the use of at least one:
- 10 (a) antibody that binds a target cell antigen; and/or
- (b) antigen that binds to an antibody (or an antigen-antibody complex) on or in a target cell
- in the reproductive tract cell sample.
- 15 21. A method as claimed in claim 20, in which an antibody is used to bind to antigens on or in the one or more target cells contained in the reproductive tract cell sample.
22. A method as claimed in claim 21, in which the antibody is capable of binding to one or more embryonic cell antigens.
- 20 23. A method as claimed in claim 21, in which an antibody is used to bind to antigens on or in one or more embryonic cells contained in the reproductive tract cell sample, and the antibody is capable of binding to one or more of:
- (a) PAX-8;
- (b) CD71;
- (c)  $\gamma$  globin (fetal);
- 25 (d)  $\zeta$  globin (embryonic);
- (e) glycophorin A;
- (f) CD 36;

- (g) Fkl-1;
- (h) EPO-R;
- (i) CDw50;
- (j) CD45;
- 5 (k) Human chorionic gonadotrophin;
- (l) Placental alkaline phosphatase;
- (m) Human placental lactogen;
- (n) Folate binding protein (LK26); or
- (o) a HLA antigen.
- 10 24. A method as claimed in any of the preceding claims, in which the genetic analysis of the one or more target cells isolated from the reproductive tract cell sample comprises the use of either or both:
- (a) genetic amplification techniques; and/or
- (b) genetic identification techniques.
- 15 25. A method as claimed in claim 24, in which the amplification technique comprises or utilises one or more of the following:
- (a) polymerase chain reaction;
- (b) comparative genome hybridisation;
- (c) single nucleotide polymorphism genotyping;
- 20 (d) fluorescent in situ hybridisation;
- (e) whole genome amplification;
- (f) rolling circle amplification; and/or
- (g) linear amplification

26. A method as claimed in claim 25, in which the techniques (a) to (f) are carried out:
- (a) sequentially, with technique (a) being used first; or
  - (b) in any other sequence.
- 5 27. A method as claimed in claim 24, in which the genetic identification technique comprises or utilises one or more of the following:
- (a) DNA fingerprinting;
  - (b) Nucleic acid separation techniques;
  - (c) polymerase chain reaction;
  - 10 (d) multiplex polymerase chain reaction;
  - (e) comparative genome hybridisation;
  - (f) single nucleotide polymorphism genotyping;
  - (g) fluorescent in situ hybridisation;
  - (h) reverse transcriptase-polymerase chain reaction;
  - 15 (i) whole genome amplification; and/or
  - (j) rolling circle amplification.
28. A method as claimed in claim 27, in which the techniques (a) to (i) are carried out:
- (a) sequentially, with technique (a) being used first; or
  - 20 (b) in any other sequence.
29. A method as claimed in any of the preceding claims, in which the results of the performance of the method are analysed.
30. A method as claimed in any of the preceding claims, in which the performance of at least one of the steps comprising the method is automated or semi-automated.
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- 5 31. A method as claimed in any of the preceding claims, in which the performance of the method is used to identify or diagnose the presence of at least one predetermined genetically mediated condition in the one or more target cells contained in or isolated from the reproductive tract cell sample.
- 10 32. A method as claimed in claim 31 when appended to claim 3, in which the predetermined genetically mediated condition comprises one or more of the following:
- (a) Genetic syndromes;
  - (b) Cystic fibrosis;
  - (c) Factor V Leiden mutation;
  - (d) Human A blood grouping;
  - (e) Human B blood grouping;
  - (f) Human O blood grouping;
  - 15 (g) Human Rh positive blood factor grouping;
  - (h) Human Rh negative blood factor grouping;
  - (i) Tay Sachs disease
  - (j) Fabry disease
  - (k) Haemachromatosis
  - 20 (l) Haemoglobinopathies
  - (m) The DNA fingerprint of an embryo borne by the subject; and
  - (n) The sex of an embryo borne by the subject.
- 25 33. A method as claimed in Claim 31 when each genetic condition can be assessed individually, sequentially or simultaneously with any other genetic condition or combination of other genetic conditions.
34. A method as claimed in any of claims 1 to 33, in which the time between:

- (a) collection of the reproductive tract cell sample; and
- (b) receiving the results of analysis of the reproductive tract cell sample is between six hours and seven days.
35. A method as claimed in claim 34, in which the time between:
- 5 (a) collection of the reproductive tract cell sample; and
- (b) receiving the results of analysis of the reproductive tract cell sample is within 48 hours from the time of collecting the reproductive tract cell sample.
36. A method as claimed in claim 34, in which the time between:
- 10 (a) collection of the reproductive tract cell sample; and
- (b) receiving the results of analysis of the reproductive tract cell sample is within 24 hours from the time of collecting the reproductive tract cell sample.
37. A method as claimed in claim 36, in which the time between:
- 15 (a) collection of the reproductive tract cell sample; and
- (b) receiving the results of analysis of the reproductive tract cell sample is within 6 hours from the time of collecting the reproductive tract cell sample.
38. A method as claimed in any of the preceding claims, in which an analyst is able to perform the method at least 10 times in a period of 24 hours from the collection of a first reproductive tract cell sample from a subject.
- 20 39. A method as claimed in claim 38, in which the analyst is able to perform the method at least 20 times in a period of 24 hours from the collection of a first reproductive tract cell sample from a subject.
40. A method as claimed in claim 39, in which the analyst is able to perform the method at least 50 times in a period of 24 hours from the collection of a first reproductive tract cell sample from a subject.
- 25 41. A method of analysing the genetic characteristics of a target cell sample taken from the reproductive tract of a female subject, substantially as



described in this specification, and with reference to the examples given and the accompanying drawings.

- 5      42.      A method of identifying or diagnosing the presence of at least one predetermined genetically mediated condition in target cells contained in or isolated from a reproductive tract cell sample taken from a female subject, substantially as described in this specification, and with reference to the examples given and the accompanying drawings.